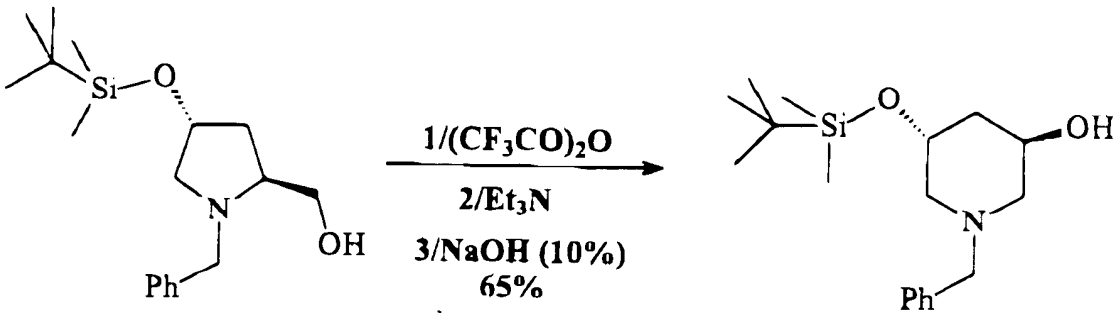

15 16

As this molecule was optically active, a C-2 axis of symmetry was present in the molecule and proved that the absolute configuration at C-3 was (R).

The first step of this ring expansion is probably the esterification of the alcohol by the trifluoroacetic anhydride and the formation of a quaternary ammonium salt. Without any triethylamine, no rearrangement is observed. When the triethylamine is added, an azidirinium ion is probably formed and the attack of the trifluoroacetate anion takes place either intra- or intermolecularly.--

REMARKS

Claims 1-26, all the pending claims, stand rejected.

The specification has been amended to incorporate portions of Cossy *et al.* (Tetrahedron Lett., **1995**, 36, 549), cited on page 91 of the application as filed. All references cited in the application were specifically incorporated by reference on page 150, line 35 to page 151, line 1. Pursuant to MPEP 608.01(p), Applicant's undersigned representative has certified in a concurrently submitted declaration that the amendatory material is the same as that material that was previously incorporated by reference. Accordingly, no new matter has been added by the foregoing amendment.

Rejections under 35 U.S.C. §112, first paragraph

Claims 1-26 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly "containing subject matter which was not described in the specification in such a way as to enable one skilled in the art . . . to make the invention." (Final Rejection at page 2). The Advisory Action states that the description of starting material in Example 77, citing Cossy *et al.*, is essential material and therefore may not be incorporated by reference. Applicants respectfully traverse this rejection.

As will be recognized, the enablement requirement of §112 is satisfied so long as a disclosure contains sufficient information that persons of ordinary skill in the art having the disclosure before them would be able to make and use the invention. *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) (the legal standard for enablement under §112 is whether one skilled in the art would be able to practice the invention without undue experimentation). Applicants respectfully submit that those of skill in the art would indeed be able to make and use the claimed inventions, including those described in Example 77.

However, in an attempt to further the prosecution of this application, Applicants have amended the specification to include the material requested by the Examiner. As discussed above, Applicants have amended the specification to incorporate portions of Cossy *et al.*

(Tetrahedron Lett., **1995**, 36, 549), cited on page 91 of the application as filed.[1] Pursuant to MPEP 608.01(p), Applicants have also certified in a concurrently submitted declaration that the amendatory material is the same as that material that was previously incorporated by reference.

The foregoing represents a *bona fide* attempt to advance the present case to allowance. Applicants respectfully request early notification of the same. Applicants invite the Examiner to contact the undersigned at (215) 564-8338 to clarify any unresolved issues raised by this response.

Respectfully submitted,

Gwilym John Owen Attwell
Registration No. 45,449

Date: January 16, 2001

WOODCOCK WASHBURN KURTZ
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Philadelphia, PA 19103
(215) 568-3100

Attachments:

Copy of pages from 1994 Aldrich catalog

[1] Applicant notes that the starting material (4R)-hydroxy-L-proline was commercially available from Aldrich Chemical Company prior to the filing date of the present application. See page 808 of 1994 Aldrich catalog, H5,440-9, a copy of which is enclosed herewith.

28,703-2 **3α-Hydroxy-5α-pregnan-20-one,** 98+% [*516-54-1*] (allopregnan-3α-ol-20-one) FW 318.50 mp 174-175° $[\alpha]^{25}$ + 98° (c = 0.8, C_5H_5OH) *Beil.* 8(3),621 *Merck Index* 11,274 *FT-NMR* 1(3),576C *SI* 416,C,3 *Safety* 2,2832A *R&S* 1(2),2858K *RTECS#* TU4383000 Disp. A — 1g 5g

Hydroxypregn-4-ene-3,20-dione, see Hydroxyprogesterone

28,619-2 **20α-Hydroxypregn-4-en-3-one** [*145-14-2*] FW 316.48 mp 165-166° *Beil.* 8(3),947 *FT-NMR* 1(3),580B *SI* 416,C,6 *R&S* 1(2),2861G *RTECS#* TU6569000 Disp. A — 5mg 25mg

H5,420-4 **(+)-11α-Hydroxyprogesterone,** 95% [*80-75-1*] (11α-hydroxypregn-4-ene-3,20-dione) FW 330.47 mp 165-166° $[\alpha]^{25}$ + 179.5° (c = 1, $CHCl_3$) *FT-NMR* 1(3),582B *FT-IR* 1(2),1054A *SI* 416,B,6 *R&S* 1(2),2861M Disp. A — 1g 25g

28,620-6 **11β-Hydroxyprogesterone,** 98% [*600-57-7*] (11β-hydroxypregn-4-ene-3,20-dione) FW 330.47 mp 187-189° *Beil.* 8(3),2501 *FT-NMR* 1(3),582C *SI* 416,C,8 *R&S* 1(2),2861N *RTECS#* TU5058000 Disp. A — 10mg 50mg

28,621-4 **16α-Hydroxyprogesterone,** 97% [*438-07-3*] (16α-hydroxypregn-4-ene-3,20-dione) FW 330.47 mp 224-228° $[\alpha]^{25}$ + 150° (c = 0.65, $CHCl_3$) *Beil.* 8(4),2188 *FT-NMR* 1(3),583A *SI* 416,D,8 *R&S* 1(2),2861O Disp. A — 1mg 5mg

28,622-2 **17α-Hydroxyprogesterone,** 98% [*68-96-2*] (17α-hydroxypregn-4-ene-3,20-dione) FW 330.47 mp 219-220° $[\alpha]^{25}$ + 90° (c = 1, $CHCl_3$) *Beil.* 8(3),2503 *Merck Index* 11,4773 *FT-NMR* 1(3),583B *SI* 416,A,7 *Safety* 2,1955D *R&S* 1(2),2863A *RTECS#* TU5060000 Disp. A — 5g

42,017-4 **cis-3-Hydroxy-DL-proline,** 97% [*4298-05-9*] FW 131.13 mp 232° (dec.) *Beil.* 22(5),5,4 — 10mg

21,994-0 **cis-4-Hydroxy-D-proline,** 99% [*2584-71-6*] [(2*R*,4*R*)-(+)-4-hydroxy-2-pyrrolidinecarboxylic acid] FW 131.13 mp 243° (dec.) $[\alpha]\beta$ + 58° (c = 2, H_2O) *Beil.* 22(1),546 *Merck Index* 11,4775 *FT-NMR* 1(1),587B *FT-IR* 1(1),584A *SI* 91,B,9 *R&S* 1(1),883M Disp. A — 250mg 1g

21,995-8 ★ **cis-4-Hydroxy-L-proline,** 99% (*618-27-9*) [(2*S*,4*S*)-(-)-4-hydroxy-2-pyrrolidinecarboxylic acid] FW 131.13 mp 257° (dec.) $[\alpha]\beta$ -59.0° (c = 2, H_2O) *Beil.* 22(1),546 *Merck Index* 11,4775 *FT-NMR* 1(1),587C *FT-IR* 1(1),584B *SI* 91,C,9 *R&S* 1(1),883N Disp. A — 50mg 250mg

H5,440-9 ★ **trans-4-Hydroxy-L-proline,** 99+% [*51-35-4*] [(2*S*,4*R*)-(-)-4-hydroxy-2-pyrrolidinecarboxylic acid] FW 131.13 mp 273° (dec.) $[\alpha]^{25}$ -75.6° (c = 1, H_2O) *Beil.* 22,191 *Merck Index* 11,4775 *FT-IR* 1(1),583D *SI* 92,A,1 *R&S* 1(1),663O Disp. A — 2.5g 10g 25g 100g
A constituent of collagen. *Arch. Biochem. Biophys.*, 270, 294 (1989).

38,980-3 ★ **3-Hydroxy-1-propanesulfonic acid, sodium salt,** tech., 80% [*3542-44-7*] $HO(CH_2)_3SO_3Na$ FW 162.15 mp 260° (dec.) *Beil.* 4,16 *FT-NMR* 1(1),1432B *FT-IR* 1(1),895D *R&S* 1(1),1057K — 25g 100g

3-Hydroxy-1-propanesulfonic acid γ-sultone, see 1,3-Propane sultone

2-Hydroxypropionitrile, see Lactonitrile

23,635-7 ★ **3-Hydroxypropionitrile,** 99+% [*109-78-4*] (ethylene cyanohydrin, hydracrylonitrile) $HOCH_2CH_2CN$ FW 71.08 mp -46° bp 226° $n\beta$ 1.4230 d 1.041 Fp > 230°F(110°C) *Beil.* 3,298 *FT-NMR* 1(1),1371C *FT-IR* 1(1),852C *Safety* 2,1956B *R&S* 1(1),999I *RTECS#* MU5250000 Disp. A *IRRITANT* — 50g

10,992-4 ★ **3-Hydroxypropionitrile,** 97% [*109-78-4*] (ethylene cyanohydrin, hydracrylonitrile) $HOCH_2CH_2CN$
Contains ≤3% ethylene glycol — 5g 250g 1kg

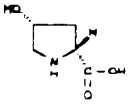
H5,510-3 **2'-Hydroxypropiophenone,** 97% [*610-99-1*] $HOC_6H_4COC_2H_5$ FW 150.18 bp 115°/15mm $n\beta$ 1.5480 d 1.094 Fp > 230°F(110°C) *Beil.* 8,102 *FT-NMR* 1(2),856A *FT-IR* 1(2),40C *SI* 240,C,7 *Safety* 2,1956C *R&S* 1(2),1847K Disp. A *IRRITANT* — 100g 500g

H5,540-5 ★ **4'-Hydroxypropiophenone,** 98% [*70-70-2*] $HOC_6H_4COC_2H_5$ FW 150.18 mp 147.5-148.5° *Beil.* 8,102 *Merck Index* 11,6992 *FT-NMR* 1(2),861C *FT-IR* 1(2),44C *SI* 241,D,4 *Safety* 2,1956D *R&S* 1(2),1651C *RTECS#* UH1925000 Disp. A *IRRITANT* — 100g 500g

37,093-2 **Hydroxypropyl acrylate,** 95%, mixture of isomers [*999-61-1*] $H_2C=CHCO_2C_3H_6OH$ FW 130.14 bp 77°/5mm $n\beta$ 1.4450 d 1.044 Fp 193°F(89°C) *Beil.* 2(4),1489 *FT-NMR* 1(1),1044B *SI* 108,D,8 *R&S* 1(1),753K *RTECS#* AT1925000 Disp. C *HIGHLY TOXIC IRRITANT* — 1L

19,188-4 ★ **Hydroxypropyl cellulose** [*9004-64-2*] *Merck Index* 11,4778 *FT-IR* 1(2),1179A *SI* 451,D,4 *Safety* 2,1957A *RTECS#* NF9050000 Disp. A
Powder. Average M.W. 100,000 — 5g 100g 250g

19,188-2 ★ **Hydroxypropyl cellulose** [*9004-64-2*]
Powder. Average M.W. 370,000 — 5g 100g 250g



21,994-0